**IN THE SPECIFICATION:**

- On Page 1, please replace the "Related Appliations" paragraph inserted by preliminary amendment at the time of filing with:

CROSS-REFERENCE TO RELATED APPLICATIONS

~~The present application is a Continuation of USSN 08/854,039, filed May 9, 1997, which is a Continuation of USSN 08/765,702, filed January 15, 1997, which is a National filing of PCT/US95/07361, which claims priority to USSN 08/275,983, filed September 13, 1994, which is a Continuation-in Part of 08/179,045 filed January 7, 1994.~~ This application is a continuation of U.S. Patent Application No. 08/854,039, filed May 9, 1997, now U.S. Patent No. 6,355,774, which is a continuation of U.S. Patent Application No. 08/765,702, which is the national stage filing under 35 U.S.C. 371 of International Application No. PCT/US95/07361, filed June 7, 1995, which is a continuation-in-part of U.S. Patent Application No. 08/275,983, filed July 15, 1994, now U.S. Patent No. 5,688,665, which is a continuation-in-part of U.S. Patent Application No. 08/179,045, filed January 7, 1994. International Application No. PCT/US95/07361 was published under PCT Article 21(2) in English.

- On page 16, please replace the paragraph starting at line 7 with the following text:

Mammalian Kip1 sequences, and comparison with Cip1/WAF1. A. Amino acid sequences deduced from Kip1 cDNAs from mink (mk), mouse (m) and human (h) (SEQ ID NOS: 6, 4, and 2). Identical amino acids are indicated by dots. The available mink sequence is incomplete at the C-terminus. Peptide sequences obtained from purified Kip1 (SEQ ID NO: 2) are underlined. Thick underlining indicates the two sequences that served to design degenerate oligonucleotides for PCR. The first occurrence of thick underlining is directed to mink kip1 and mouse kip1 sequence NLFGPVNHEELTR (SEQ ID NO: 26) and human kip1 sequence NLFGPVDHEELTR (SEQ ID NO: 27). The sequence LFGPVN (SEQ ID NO: 22) within NLFGPVNHEELTR and the sequence LFGPVD (SEQ ID NO: 25) within NLFGPVDHEELTR respectively correspond to the longest uninterrupted stretch of identity to Cip1/WAF1 (SEQ ID NO: 24). B. Sequence

alignment between human Kipl and Cipl/WAFT. The putative bipartite nuclear localization signal in both proteins is underlined. A Cdc2 kinase consensus site present in Kipl is indicated by a thick bar.

- On pages 66 and 67, please replace the paragraphs at lines 1-37 and 1-12 respectively with the following text:

Various Kip1 tryptic peptide sequences were obtained by automated Edman degradation and used to design degenerate oligonucleotide primers for cDNA amplification by the reverse transcription-polymerase chain reaction (RT-PCR). A PCR product amplified out of reverse-transcribed Mv1Lu mRNA was used to screen a Mv1Lu cDNA library. This yielded one single positive clone that encoded the sequences obtained from the purified protein (Figure 9A). Screening of cDNA libraries from human kidney and mouse embryo with the Kip1 cDNA yielded clones of highly related sequence. The human and mouse Kip1 cDNAs (Genbank Accession Numbers U10906 and U09968 (SEQ ID NOS: 1 and 3)) had open reading frames of 594 and 591 bp, respectively, starting with an ATG codon in a favorable translation initiation context and preceded by stop codons (data not shown). Compared to these open reading frames, the mink clone (Genbank Accession Number U09966 (SEQ ID NO: 5)) was incomplete, and ended at nucleotide 534 (Figure 9A).

The Kip1 cDNA encodes a predicted protein of 198 amino acids (22,257 daltons) in human (SEQ ID NO: 2) and 197 amino acids (22,208 daltons) in mouse (SEQ ID NO: 4). These values are smaller than the 27 kd value obtained with the purified mink protein by SDS-PAGE. To resolve this discrepancy, a cDNA encoding the mouse Kip1 sequence was constructed, and tagged at the C-terminus with a hexahistidine sequence (~1 kd mass). In vitro transcription and translation of this cDNA yielded a product that bound specifically to $Ni^{++}$-NTA-agarose and migrated as a 28 kd protein on SDS-PAGE gels (Figure 8C), confirming that the cloned cDNA encodes full-length Kip1 and that this protein migrates on SDS-PAGE somewhat slower that its calculated molecular mass.

Kip1 is highly conserved and related to Cip1/WAF1

The predicted human, mouse and mink Kip1 amino acid sequences are highly related, showing

~90% identity (Figure 9A) (SEQ ID NOS: 2, 4, and 6). A Genbank search revealed that, at the amino acid level, Kip1 shows significant homology only to Cip1/WAF1. The similarity was largely limited to a 60-amino acid segment in the N-terminal half of the protein. This region was 44% identical to the corresponding region in Cip1/WAF1 (SEQ ID NO: 24) (Figure 9B). Like Cip1/WAF1, Kip1 has a putative bipartite nuclear localization signal (Dingwall and Laskey, 1991) near the C-terminus (SEQ ID NO: 2) (Figure 9B) . Yet unlike Cip1/WAF1, the Kip1 sequence does not have a putative zinc finger motif in the N-terminal region, and has a C-terminal extension of 23 amino acids that contains a consensus Cdc2 phosphorylation site (SEQ ID NO: 2) (Figure 9B).

- On pages 68 and 69, please replace the paragraph at lines 35-37 and 1-14 respectively with the following text:

Cdk Inhibitory Domain

It was investigated whether the inhibitory activity of Kip1 resided in the region of similarity to Cip1/WAF1. A 52-amino acid peptide [Kip1(28-79)] corresponding to this region in Kip1 (SEQ ID NO: 2) (Figure 10E) was produced recombinantly and purified with a C-terminal hexahistidine tag. This peptide inhibited Rb phosphorylation by cyclin A-Cdk2 with a potency that was close to that of full length Kip1 (Figure 10E) and inhibited cyclin E-Cdk2 or cyclin D2:Cdk4 less effectively. Versions of this Kip1 region missing three amino acids at the N-terminus or fifteen at the C-terminus, were much weaker as Cdk inhibitors, and deletion of seven N-terminal amino acids yielded a product with no inhibitory activity (Figure 10E). The peptide Kip1[(104-152)] (SEQ ID NO: 2) which has little sequence similarity to Cip1/WAF1 (SEQ ID NO: 24), was inactive as a Cdk inhibitor (Figure 10E).

- On pages 70 and 71, please replace the paragraph at lines 32-37 and 1-5 respectively with the following text:

A family of Cdk inhibitors

Human Kip1 encodes a protein of 198 amino acids (SEQ ID NO: 2) that is highly conserved (~90% identity) in mouse (SEQ ID NO: 4) and mink (SEQ ID NO: 6). Its most distinctive feature is a 60-amino acid region in the N-terminal half that has amino acid sequence similarity

to Cip1/WAF1 (El-Deiry et al., 1993; Harper et al., 1993; Xiong et al., 1993). Like Cip1/WAF1, Kip1 contains a potential nuclear localization signal in the C-terminal region. In Kip1, this region also contains a consensus Cdc2 kinase site that might play a role in feed-back regulation by their target kinases.